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C07D 271/07 (2006.01) *A61K 31/551* (2006.01)
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Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

Published:

— with international search report (Art. 21(3))
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

13 October 2016

(54) Title: CREATINE PRODRUGS, COMPOSITIONS AND METHODS OF USE THEREOF

(57) Abstract: The invention describes membrane permeable creatine prodrugs, pharmaceutical compositions comprising membrane permeable creatine prodrugs, and methods of treating diseases such as ischemia, heart failure, neurodegenerative disorders and genetic disorders affecting the creatine kinase system comprising administering creatine prodrugs or pharmaceutical compositions thereof. The invention also describes treating a genetic disease affecting the creatine kinase system, such as, for example, a creatine transporter disorder or a creatine synthesis disorder comprising administering creatine prodrugs or pharmaceutical compositions thereof.



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/067283**A. CLASSIFICATION OF SUBJECT MATTER****C07D 273/04(2006.01)i, C07D 271/07(2006.01)i, C07D 273/06(2006.01)i, A61K 31/5395(2006.01)i, A61K 31/4245(2006.01)i, A61K 31/551(2006.01)i, A61P 25/00(2006.01)i, A61P 25/28(2006.01)i**

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D 273/04; C07D 257/04; C07D 211/46; A61K 31/661; A61K 31/41; A61K 31/66; A61K 31/221; C07D 403/12; A23L 1/30; C07F 9/54; C07D 401/12; C07D 271/07; C07D 273/06; A61K 31/5395; A61K 31/4245; A61K 31/551; A61P 25/00; A61P 25/28

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal), STN(Registry, Caplus), Google & Keywords: creatine, oxadiazol-one, oxadiazin-one, membrane permeable, ischemia, genetic disorder

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2014-018570 A1 (SOVA PHARMACEUTICALS, INC.) 30 January 2014 See abstract; page 89.	1-14, 19-25
A	WO 2013-043580 A2 (GENCIA CORPORATION) 28 March 2013 See abstract; claim 1; page 5.	1-14, 19-25
A	WO 2010-005692 A2 (E. I. DU PONT DE NEMOURS AND COMPANY) 14 January 2010 See abstract; page 71; table 6.	1-14, 19-25
A	WO 2009-143630 A1 (NORTHERN INNOVATIONS AND FORMULATIONS CORP.) 03 December 2009 See abstract; claim 1.	1-14, 19-25
A	US 2008-0051371 A1 (ZERANGUE, N. et al.) 28 February 2008 See abstract; claim 1.	1-14, 19-25

 Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

19 August 2016 (19.08.2016)

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/067283**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 26-34
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 26-34 pertain to methods for treatment of the human body by surgery or therapy, and thus relate to a subject matter which this International Searching Authority is not required to search (PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv)).
2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Group 1: Claims 1-12, 19-25 (all partial); 13-14

Inventions related to a compound of Formula (I), Formula (III) or a pharmaceutically acceptable salt, solvate, tautomer or stereoisomer thereof.

Group 2: Claims 1-12, 19-25 (all partial); 15, 17-18

Inventions related to a compound of Formula (VI), Formula (XXX), Formula (XXXI)-(XXXV), or a pharmaceutically acceptable salt, solvate, tautomer or stereoisomer thereof.

Group 3: Claims 1-12, 19-25 (all partial); 16

Inventions related to a compound of Formula (VII) or a pharmaceutically acceptable salt, solvate, tautomer or stereoisomer thereof.

*Note: Claims 17 and 18 are worded in reference to Formula(VIII) and Formula(IX) of claim 1 respectively. However, said Formula(VIII) and Formula(IX) have not been worded in claim 1. Therefore, the observation has been carried on the assumption that claims 17 and 18 are independent claims where unity of invention is lacking.

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of any additional fees.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-12, 19-25 (all partial); 13-14

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2015/067283

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2014-018570 A1	30/01/2014	AR 091857 A1	04/03/2015
		AU 2013-293090 A1	19/02/2015
		CA 2879879 A1	30/01/2014
		CN 104662007 A	27/05/2015
		EP 2877457 A1	03/06/2015
		EP 2877457 A4	20/04/2016
		HK 1210614 A1	29/04/2016
		IN 1161 DEN2015 A	26/06/2015
		JP 2015-524807 A	27/08/2015
		KR 10-2015-0041635 A	16/04/2015
		TW 201406711 A	16/02/2014
		US 2015-0266837 A1	24/09/2015
		WO 2013-043580 A2	28/03/2013
CA 2849073 A1	28/03/2013		
CN 103889993 A	25/06/2014		
EP 2758411 A2	30/07/2014		
HK 1200459 A1	07/08/2015		
JP 2014-527969 A	23/10/2014		
US 2015-0005258 A1	01/01/2015		
WO 2013-043580 A3	27/06/2013		
WO 2010-005692 A2	14/01/2010	WO 2010-005692 A3	08/04/2010
		WO 2010-005692 A4	03/06/2010
WO 2009-143630 A1	03/12/2009	CA 2698500 A1	03/12/2009
		CA 2698500 C	27/03/2012
		US 2009-0297685 A1	03/12/2009
		US 2009-0298877 A1	03/12/2009
		US 8426395 B2	23/04/2013
US 8546369 B2	01/10/2013		
US 2008-0051371 A1	28/02/2008	US 2010-0137255 A1	03/06/2010
		US 7683043 B2	23/03/2010
		US 8202852 B2	19/06/2012